Induction of chondrogenesis from human embryonic stem cells without embryoid body formation by bone morphogenetic protein 7 and transforming growth factor beta1.

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Authors: Toshiyuki Nakagawa, Sang Yang Lee, A Hari Reddi

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Public Summary:

Scientific Abstract:
OBJECTIVE: Human embryonic stem cells (ESCs) provide an unlimited supply of pluripotent cells for articular cartilage tissue engineering and regenerative medicine applications. Articular cartilage is an avascular tissue with precise polarity and organization comprising 3 distinct functional zones: surface, middle, and deep. To date, attempts at differentiating human ESCs into articular chondrocytes have been unsuccessful. The majority of studies have focused on chondrogenic (but not specifically articular cartilage) differentiation. Furthermore, previous investigations of induction of chondrogenesis by human ESCs required embryoid body formation; however, embryoid body formation often results in heterogeneous differentiation. The present study was undertaken to determine the in vitro chondrogenic potential of bone morphogenetic protein 7 (BMP-7) and transforming growth factor beta1 (TGFbeta1)-induced human ESC differentiation toward the articular cartilage phenotype. METHODS: Dissociated single human ESCs were cultured and passaged on a gelatin-coated flask. The human ESCs were cultured as an aggregate in a pellet culture system for 14 days in basal chondrogenic medium (CM), CM with TGFbeta1, CM with BMP-7, or CM with both TGFbeta1 and BMP-7. RESULTS: The size and wet weight of the cartilage pellets and glycosaminoglycan levels increased, with the smallest, intermediate, and greatest increases, respectively, observed with CM plus TGFbeta1 treatment, CM plus BMP-7 treatment, and CM plus TGFbeta1 and BMP-7 treatment (compared with CM treatment alone). The largest size and highest weight of the pellet was in the group in which TGFbeta1 and BMP-7 were added to the medium. However, expression of the genes for cartilage-specific aggrecan and type II collagen II, as assessed by determination of messenger RNA levels, was highest in the BMP-7-treated group. Superficial zone protein (SZP)/lubricin, a marker of the superficial zone articular chondrocyte, was not detectable under identical culture conditions. CONCLUSION: These results demonstrate an efficient and reproducible model system of human ESC-induced chondrogenesis, using a novel direct plating method in which intervening embryoid body formation does not occur. Further work is needed for optimization of conditions to obtain the articular cartilage phenotype that includes the superficial zone marker as demonstrated by SZP/lubricin synthesis.